Research article

Exploring daily blood pressure fluctuations and cardiovascular risk among individuals with motor complete spinal cord injury: a pilot study

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Background: Clinically silent autonomic dysfunction with bowel and bladder care, are postulated to contribute to cardiovascular disease after chronic spinal cord injury (SCI).
Objective: We describe the frequency and severity of dysreflexic episodes, termed transient blood pressure elevations (T-BPE) over 48 hours in adults with cervical or high-thoracic motor-complete SCI.
Setting: Tertiary SCI Rehabilitation Centre in Toronto, Canada.
Participants: Individuals with chronic SCI, C1-T3 AIS A or B, >1 year post-injury, living in the community (n = 19).
Outcome Measures: Data were obtained via 48-hour ambulatory blood pressure (BP) and heart rate (HR) monitoring, with data captured at 10-minute intervals and a concurrent diary describing activities of daily living, and bladder/bowel routines. T-BPE were defined as a ≥ 40 mmHg elevation in systolic blood pressure (SBP) above the participant's supine baseline. Severe (≥ 60–79 mmHg) and Extreme ≥80 mmHg elevations in SBP were described.
Results: Thirteen participants experienced T-BPE within the assessment period, with 7/13 experiencing "severe", and 3/13 experiencing "extreme" SBP elevations. The median number of T-BPE was 8 (IQR = 3), and the mean ± SD SBP during T-BPE was 150 ± 16 mmHg, These T-BPE were verified as dysreflexic events using a conservative definition of a >40 mmHg increase in SBP, with a concurrent 10 bpm decrease in HR, above the 48-hour average SBP, yielding 12/19 participants with T-BPE.
Conclusions: T-BPE were frequent, often with severe or extreme elevations in SBP, despite few reported symptoms. Recognition and management of these dysreflexic events associated with T-BPE are needed, which may ameliorate cardiovascular disease risk.

Keywords: Spinal cord injury, Autonomic dysreflexia, Tetraplegia, Blood pressure, Cardiovascular disease

Introduction

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in individuals with chronic spinal cord injury (SCI) ahead of renal and pulmonary complications. Approximately 40% of mortality in patients with SCI comes from CVD, resulting in significant costs, both in terms of quality of life and direct medical expenses.[1,2] Reducing CVD-related morbidity and mortality is a priority for the SCI community.

An increased prevalence of multiple CVD risk factors including central obesity, dyslipidemia, inflammatory stress and glucose intolerance are higher among individuals with SCI relative to non-SCI peers.[1] However, even after adjusting for these conventional risk factors, individuals with SCI experience disproportionately high rates of CVD, including stroke.[1,2] While hypertension

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is a well-established risk factor for CVD, the role of hypertension and blood pressure (BP) regulation in CVD morbidity and mortality is poorly understood. While individuals with SCI tend to have lower resting blood pressures when compared to healthy aged-matched peers,[3–6] it has been documented that autonomic dysfunction gives rise to abnormalities in blood pressure regulation, along with other physiologic parameters.[1,7] In individuals with SCI above T6, this autonomic dysregulation leads to an acute syndrome known as autonomic dysreflexia (AD).[8]

AD is a condition characterized by marked and sustained elevations in blood pressure, headaches, compensatory bradycardia, flushing and sweating above the level of the SCI.[8,9] A systolic blood pressure (SBP) increase of greater than 20–30 mmHg above the patient's baseline is considered a dysreflexic response,[10] although most recorded episodes involve much large pressure increases with associated symptoms.[8,11] An increase in SBP of 20–40 mmHg or greater from baseline with symptoms of AD is considered diagnostic, or in the absence of symptoms, a systolic blood pressure of ≥ 150 mmHg is considered silent AD and warrants immediate intervention.[11] The severity of dysreflexic events can be quantified, with "severe" and "extreme" episodes being defined in this study as an increase in SBP from baseline of 60 mmHg and 80 mmHg, respectively.[12]

Among individuals with tetraplegia or high paraplegia, 50–90% experience hypertensive episodes related to autonomic dysregulation.[13] Common stimuli triggering elevated SBP include bladder distension and bladder catheterization, bowel care, infection, spasticity and pressure ulcers.[7,14] Limited evidence suggests that autonomic dysreflexia can occur randomly within a 24-hour period, with stronger evidence that AD occurs in response to noxious or non-noxious stimuli below the neurologic level of injury.[15] Bowel and bladder routines, pressure sore avoidance, and individualized avoidance of triggers are the mainstays for preventing severe AD.[8,14] However, these methods aim to prevent severe episodes of AD, with little attention to asymptomatic mild or moderate episodes. Blood pressure control intended to optimize long-term CVD risk has not been evaluated.

Mathias *et al.* posits that …."mild episodes of autonomic dysreflexia probably occur intermittently through the day in response to various stimuli, but often are not noticed…."[15] While the exact mechanism(s) which elicit autonomic hyperactivity are unclear, there is mounting evidence supporting persistent autonomic changes, which produce hypertensive events, on a daily basis.[6,8,16] The authors suggest these unrecognized dysreflexic events may contribute to elevated rates of cardiometabolic disease including heart attack, stroke and other cardiovascular sequelae particularly when combined with prevalent metabolic syndrome. Many SCI practitioners have observed the phenomenon of frequent dysreflexic-type events, such as facial flushing and transient hypertension with reflex voiding. Despite the frequency of these observations, little has been published describing this clinical phenomenon or clinical implications. While hypertensive episodes from autonomic dysfunction are known to occur in individuals after SCI, the literature does not address the frequency and magnitude of these events, nor their clinical significance. Further, recent data suggests that excessively low blood pressure is also problematic.[3] Several studies document blood pressure elevations in response to various stimuli such as bladder contractions/voiding,[17] but the literature is silent on the frequency and significance of blood pressure elevations from triggers associated with daily routines such as transfers, bowel and bladder care, and other activities of daily living.

This study aims to: 1) Describe the frequency of transient-blood pressure elevations (T-BPE) in individuals with high thoracic and cervical motor complete spinal cord injury living in the community; 2) Characterize the severity of T-BPE as "severe" (≥6–79 mmHg above baseline SBP) and "extreme" (≥80 mmHg above baseline SBP)[12]; 3) Verify the autonomic origin of observed T-BPE by identifying episodes of increased SBP with a concurrent decrease in heart rate (HR) ≥10 beats per minute; and, 4) Explore the associations between T-BPE with an individual's bowel and bladder routines/events. For the purposes of this study, a transient-blood pressure elevation (T-BPE) was *a priori* defined as a ≥30 mmHg increase in SBP above the participant's baseline blood pressure. This threshold value derives from the range provided by the Paralyzed Veterans of America guidelines for the diagnosis of autonomic dysfunction, and will be the topic of further discussion.[11] During analysis of the data a more conservative threshold for T-BPE of ≥40 mmHg was subsequently adopted. These objectives were originally formulated using a fasting supine blood pressure as a baseline. However, an alternative and more conservative baseline, derived from the 48-hour average SBP was included to address objective 3 and to provide a conservative comparison. We hypothesized that individuals with cervical or high thoracic motor complete SCI experience frequent and severe T-BPE associated with self-care activities (voiding, defecating, orgasm, ejaculation, etc.), and that these T-BPE are associated with a

concomitant decrease in heart rate in keeping with their dysreflexic etiology.

Methods

This cross-sectional study was conducted at Lyndhurst Centre, Toronto Rehabilitation Institute-University Health Network, Toronto, Canada with approval of the University Health Network Research Ethics Board (TRI REB #: 11–053). Twenty-one adult men and women between the ages of 19 and 60 years of age with chronic (≥one year post-injury) cervical or high thoracic motor complete traumatic spinal cord injury (C1–T3, AIS A or AIS B) living in the community were recruited via a poster campaign and staff referral. Exclusion criteria included premorbid or current hypertension, resting SBP >150 mmHg, or a resting diastolic blood pressure (DBP) <40 mmHg, untreated autonomic dysreflexia, changing neurologic status (i.e. syrinx), ischemic heart disease; hypertrophic cardiomyopathy, severe chronic obstructive pulmonary disease (requiring oral steroids/home oxygen), severe aortic stenosis, diaphragmatic pacer; or an active infection, at the time of enrolment.

Recruitment was through a poster campaign, by letter of invitation sent to a database of consenting prior research participants, and by outpatient clinic staff referral at Toronto Rehabilitation Institute – Lyndhurst Centre. Consent was obtained, and participant eligibility confirmed through completion of a medical history, chart review and physical examination.

Screening examinations were performed, including neurologic (ISNCSCI) and cardiopulmonary assessments. Demographic and impairment data were collected, along with socio-demographic data, lifestyle risk factors, symptom inventories, health behaviours, concurrent medications, and medical comorbidities. Once screening confirmed eligibility, average supine BP was collected in order to establish a baseline blood pressure reading. Prior to the baseline SBP assessment, participants were instructed to fast and abstain from caffeine, nicotine or rigorous exercise for 12 hours. Participants maintained their usual medication regimen. In order to establish the baseline BP, supine BP measurements were recorded after ten minutes of rest, with a total of three measurements taken at two-minute intervals. A mean BP was then calculated from these three measurements to establish the participant's supine baseline BP.

Participants were provided with an ambulatory BP/HR monitor from Sunnybrook Hospital which recorded blood pressure (SBP and DBP), HR and mean arterial pressure (MAP) at 10-minute intervals consecutively over 24 hours. This 24-hour monitoring was repeated on two occasions (either on two consecutive days, or on two separate days within a two-week period) for a total of 48 hours. Participants were asked to complete a paper or electronic diary to record the time of daily activities including bowel/bladder routines, transfers, noxious stimuli/pain or other events. The time on the ambulatory monitor was confirmed to align with the participant's watch or electronic device by a laboratory technician at the time of monitoring. Participants were requested to capture at least one bowel routine within the 48-hour period to ensure potential fluctuations in SBP, DBP and HR between "bowel days" and "non-bowel days" were captured. From this 48-hour BP data, an alternative baseline SBP was established by calculating the mean of all the BP measurements recorded in the 48-hour period.

The supine baseline BP value was used as the baseline SBP for calculating the frequency and severity of T-BPE as per the original hypothesis. To provide a conservative estimate of T-BPE, the upper threshold (≥40 mmHg SBP increase above baseline) was adopted, contrary to the original project hypothesis (≥30 mmHg).[11] This strategy was adopted to ensure that the number of episodes was not overestimated, as the average supine SBP was lower and more variable than the 48-hour average SBP. A T-BPE was defined as a ≥40 mmHg SBP increase above baseline; "severe" elevation was defined as a ≥60 mmHg SBP increase above the supine baseline SBP; while and "extreme" elevation was ≥80 mmHg SBP increase above baseline.[12] These categories were adopted from the sited reference, with the modification of "extreme" replacing "malignant". To further validate the existence of T-BPE, the 48-hour average SBP was used in a secondary analysis along with HR data, to document whether the T-BPE were associated with a decrease in HR of ≥10 beats per minute from the 48-hour average, in order to provide a highly conservative estimate of T-BPE frequency.

Data were collected on bladder and other potential triggers of T-BPE, including transfers, painful stimuli, eating, and sexual activity, but are not reported here.

Data were analyzed using SPSS software (version 22, IBM Corp., Armonk, NY, USA) and were validated by random sample comparison to original data. The assumption of normality of SBP in the sample population was assessed, and key outcomes were evaluated for outliers. Where outliers were identified, those participants were removed from all analyses (for a sample size of n = 19 for all objectives). Appropriate descriptive statistics for continuous and categorical variables were

used to characterize baseline demographic, impairment and medical factors (Table 1), the frequency and severity of T-BPE, severe and extreme T-BPE. To characterize T-BPE, the frequency of T-BPE in 48 hours were grouped into three categories: "absent" (0 T-BPE), "infrequent" (1–8 T-BPE) or "frequent" (≥9 T-BPE) based on the median of participants experiencing T-BPE. Descriptive statistics were used to characterize the severity of T-BPE and to identify T-BPE with concomitant decreases in HR. Limited univariate correlations between key bowel data variables (symptom inventory, bowel dysfunction, and T-BPE with bowel routine) and the primary outcome (T-BPE) were conducted. No adjustment for multiple testing was made, and $P \leq 0.05$ was considered significant for the above parametric tests.

Results

Twenty participants completed study related data collections, two participants withdrew due to logistical constraints prior to continuous BP monitoring, and one participant was withdrawn due to diagnosis of severe hypertension upon completion of 48-hour ambulatory blood pressure monitoring, suggestive of untreated AD. The data from this participant was not included in the analyses as their average 48-hour SBP was >160 mmHg, which was more than 3 standard deviations (SDs) above the group mean SBP. An additional participant was excluded from the analyses as their number of T-BPE fell more than 3 SDs above the population mean, likely due to a low supine baseline blood pressure (>30 mmHg below their 48-hour average). Two participants reported a prior diagnosis of hypertension, but were not taking antihypertensive medication, and had no documented SBP measures >120 mmHg, thus, their data was included in the analysis.

Results were analyzed for outliers and the blood pressure data (SBP) was found to have a normal distribution. Table 1 displays the demographic characteristics, medical comorbidities and potential predictors of AD among study participants are reported (Table 1). The cause of injury for this sample included motor vehicle accidents (n = 9), sports (n = 4), missing (n = 3), fall (n = 2) and gunshot (n = 1). Alcohol consumption was reported in nine of nineteen participants at a mean of 2.6 servings per week. Four of nineteen participants were current smokers, while thirteen of nineteen participants currently consumed caffeine and three of thirteen consumed ≥3 cups per day. Four of nineteen participants were current marijuana users. No participants reported using beta blockers or other blood pressure medications.

The bladder routines for cohort members included intermittent catheterization (8/12 participants), indwelling catheters (3/12), and reflex voiding (1/12). Nine of fifteen participants used digital ano-rectal stimulation and eight used suppositories, while two used straining to facilitate bowle evacuation. Select Autonomic Standards descriptors for cohort members included ten of eighteen participants having experienced hypotension, with fifteen of eighteen reporting orthostatic hypotension, and fifteen reporting previous autonomic dysreflexia. Six of sixteen had experienced bradycardia, with two experiencing documented tachycardia.

The frequency and prevalence of T-BPE

SBP data were analyzed and baseline values were established for each participant (Table 2).

The majority of participants (13/19) had one or more SBP elevation meeting the cut-off for a T-BPE (≥40 mmHg), with the number of T-BPE by participant shown in (Fig. 1). The median number of T-BPE for all participants (n = 19) was 3 (IQR 0, 14) in 48 hours. The "frequent" T-BPE group consisted of 6 participants, with a median number of elevations of 25 (IQR 13,35) T-BPE/48 hrs, as shown in Figure 2. The infrequent T-BPE group had 7 participants, with a median number of 3 (IQR 1,7) T-BPE/48 hrs, and the remaining 6 participants experienced no T-BPE.

The severity of T-BPE

The increase in SBP was *a priori* classified as severe (60–80 mmHg) and extreme (>80 mmHg). Seven of nineteen (36.8%) participants experienced severe elevations, while 3/19 (15.8%) experienced extreme elevations (Fig. 3). The infrequent T-BPE group had a median of 1.5 (IQR 1,2, N = 2) severe elevations, while the "high" T-BPE group had 4 (IQR 4,7, N = 5) severe elevations. The "frequent" group had all 3 extreme elevations. To further characterize the severity of T-BPE, 4 participants had SBPs of 180 mmHg or higher during a T-BPE. The mean SBP during a T-BPE was 150 ± 16 mmHg.

Verify the autonomic origin of observed T-BPE

The new finding of a large number of T-BPE at the 40 mmHg level prompted a secondary analysis toward validating this result. The more conservative 48-hour average SBP was substituted as a baseline, and run at the 30 mmHg and 40 mmHg levels. These T-BPE's were narrowed to episodes where a concurrent decrease in heart rate (from the 48-hour HR average) of 10 beats per minute were observed. T-BPE with decreased HR occurred in 12/19 participants at the ≥30 cut-off, and 9/19 participants at the ≥40 mmHg cut-off, as shown

Table 1 Descriptive parameters of key demographic and medical variables (N = 19)

Variable	Mean (SD)
Age (years)	45.0 (SD 8.2)
Years since injury (years)	19.1 (SD 9.4)
Total motor score (/100)	25.6 (SD 13.9)
Variable	**N (% distribution)**
Neurologic level of injury	
• C1–C4 AIS A or B	3 (15.8%)
• C5–C8 AIS A or B	12 (63.2%)
• T1–T3 AIS A or B	4 (21.1%)
Sex (Male)	15 (78.9%)
Diabetes	2 (10.5%)
Hypercholesterolemia	5 (26.3%)
Family history of CAD	11 (57.9%)
Metabolic syndrome	1 (5.3%)
Obesity	3 (15.8%)

in Figure 4 ordered by T-BPE using the original supine baseline.

Association of T-BPE with bowel and bladder events

Eleven participants recorded one or two bowel routines during the 48-hour ambulatory monitoring period, of which 7 experienced a T-BPE during or within 10 minutes of starting or finishing their bowel routine. Of these, five had T-BPE with a decrease in HR during their bowel routine. The diary captured the start and finish times of each of these events, although the accuracy of reporting varied depending on the diligence of the participant. A significant correlation was observed between bowel-related dysreflexic episodes and the T-BPE with reduced HR ($r = 0.648$, $P = 0.031$), while the number of T-BPE without a decrease in HR revealed a non-significant trend ($r = 0.540$, $P = 0.086$).

Discussion

The frequency and prevalence of T-BPE

This study aimed to characterize the frequency of T-BPE in individuals with SCI. As illustrated in Figure 1, we found that using a supine baseline SBP, the majority (13/19) of participants experienced elevations in SBP consistent with AD. Among these 13, the 6/13 in the "high" group had a median of 25 (IQR 13,35) T-BPE while 7/13 in the "low" group had 3 (IQR 1,7) T-BPE. A supine baseline SBP was used to provide a high/conservative estimate of baseline

Table 2 Individual and mean results from 48 hour ambulatory blood pressure assessments (SBP), supine baseline SBP, and sitting baseline SBP (first visit SBP)(n = 19)

Subject	48-hour mean SBP (mmHg)	Supine baseline SBP (mmHg)	Random sitting SBP (mmHg)
1	114.87	100.7	95.0
2	116.58	98.8	105.0
3	125.94	116.8	105.0
4	117.95	93.0	90.0
4	117.55	104.7	115.0
6	89.95	70.0	75.0
7	111.68	125.0	105.0
8	116.59	96.7	104.0
9	107.71	98.7	88.0
10	99.25	115.0	102.0
11	98.55	91.3	102.0
12	99.94	98.7	96.0
13	118.99	110.7	118.0
14	109.33	108.0	104.0
15	120.44	128.0	128.0
16	94.74	92.0	88.0
17	95.10	91.3	58.0
18	103.20	124.0	96.0
19	105.58	109.0	94.0
Group Mean	109 (SD 10)	104 (SD14)	98.3 (SD 15)

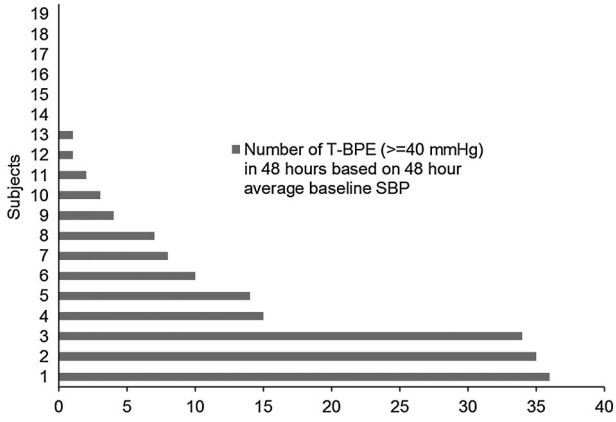

Figure 1. Histogram of Number of T-BPE (≥40 mmHg, using supine SBP baseline, in 48 hours) for each participant

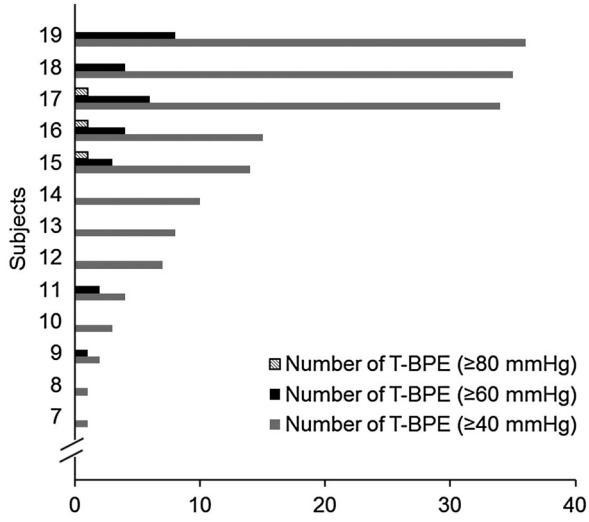

Figure 3. Histogram characterizing severity of T-BPE (≥40 mmHg, Severe ≥60 mmHg, Extreme ≥80 mmHg) from the participant's supine baseline SBP

pressure, as orthostatic hypotension produced during a sitting measure could result in overestimation of the measured number of T-BPE. The sitting SBP data we collected was lower in this instance [98 mmHg (SD 15 mmHg)]. The mean supine baseline pressure was 104 mmHg (SD 14 mmHg), which is comparable to the 48-hour average SBP [109 mmHg (SD 10 mmHg)], and in keeping with other studies in similar SCI populations.[3,6,18]

In able-bodied individuals, blood pressure varies during the day in response to a variety of internal or external stimuli. For example, blood pressure increases during exercise through autonomic nervous system activity. Further during resistance training, with 80% of one-repetition maximum, able-bodied individuals have transient increases in SBP of more than 40mmHg and 70 mmHg in untrained middle aged men and young men respectively.[10] However, this sympathetically-driven response would not typically be seen in this study population.[6] Further, large sustained SBP elevations (≥40 mmHg) would be uncommon in healthy individuals with the types of activities performed by participants during the study period. Blood pressure variability within 24 hours, assessed as coefficient of variation in able-bodied people, is smaller than in people with tetraplegia who have recently experienced episodes of AD.[4] Accordingly, the authors propose that T-BPE would be infrequent in the study population from usual daily activities.

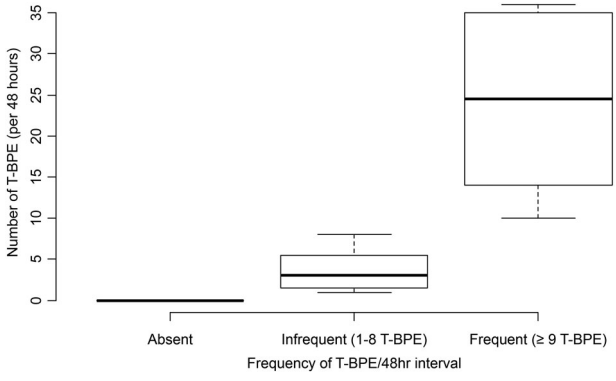

Figure 2. Histogram of Category of Transient Blood Pressure Episodes (T-BPE) over 48 hours versus number of T-BPE (elevations of 40 mmHg SBP) including 95% CI. Absent; 0 T-BPE in 48 hours (n = 6); Infrequent: 1–8 T-BPE in 48 hours (N = 7); and Frequent: ≥9 T-BPE in 48 hours (N = 7)

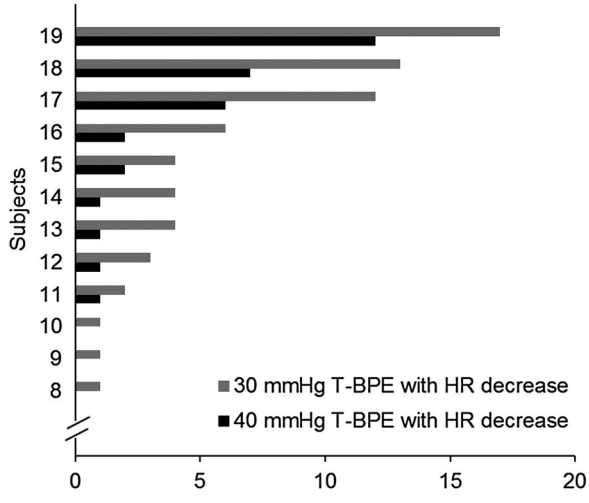

Figure 4. Histogram of T-BPE occurring with relative bradycardia (≥30 mmHg and ≥40 mmHg T-BPE using 48-hour average SBP baseline, with associated >10 bpm decrease in heart rate) by participant

The severity of T-BPE

Based on the *a priori* classification of T-BPE elevations adopted for this project, the numbers of participants with severe (60–79 mmHg) elevations was 7/19, with 3 participants having extreme (≥ 80 mmHg) T-BPE. Severe and extreme T-BPE are likely to be clinically significant. Regrettably, a detailed assessment of the duration of these severe episodes was not feasible due to HR and BP sampling at 10 minute intervals.

While the number of T-BPEs varied by subject, the average T-BPE approached the 150 mmHg threshold where pharmacologic treatment for AD is typically considered.[11] The five participants whose average SBPs during T-BPE was over 150 mmHg had an average of 13 measurements qualifying as T-BPE (at 10-minute intervals). This accounts for a cumulative average of over two hours (per 48 hours) during which their average blood pressure was above the threshold conventionally considered for pharmacologic treatment.[8] Extrapolated over days and weeks, these elevations may contribute to elevated cardiovascular disease risk. At this time, it is not clear whether the severity of SBP elevation is best accounted for by the magnitude or duration of elevation.

While a portion of the study population had a relatively low number of events, these participants should not be overlooked, particularly in light of the conservative T-BPE estimate produced through a high SBP threshold, the potential bias introduced by some participants having a relatively high baseline SBP, and the frequency potentially being unrelated to the severity of T-BPE observed. The "infrequent" T-BPE group included two participants with "severe" elevations, suggesting that both the number and magnitude of elevations may be clinically relevant. Moreover, the "infrequent" T-BPE group may include some higher risk individuals than might otherwise be inferred, due to the severity of their hypertensive episodes.

Verifying T-BPE as dysreflexic events: evaluating concurrent bradycardia

The finding of a substantial number of T-BPE with concomitant decreases in HR suggests that the captured episodes are likely dysreflexic episodes. While a number of potential confounding events could cause isolated BP fluctuations, the presence of concurrent bradycardia suggests these events to be autonomic in origin. Dysreflexic events are known to occur with elevated HRs,[16] although this would be less common and could reflect other causes of elevated SBP. The number of events with associated bradycardia would likely underestimate total T-BPE. Further, the more conservative 48-hour average SBP was used for this baseline. These combined HR and T-BPE episodes occurred at both the 30 mmHg and 40 mmHg SBP thresholds.

Association of T-BPE with bowel and bladder events

A significant correlation was seen in the bowel diary data between participants experiencing a T-BPE during their bowel routine and having one or more T-BPE with reduced HR. With bowel and bladder routines being two of the primary causes of AD, these results further suggest that the observed episodes are autonomic in nature, not random variations in blood pressure.

Bowel routines in this population span a relatively long period of time, typically at least 30 minutes, often 60 or 90 minutes. They are therefore less sensitive to time coding errors. This is confounded by the possibility of T-BPE occurring during a bowel routine by chance or due to another precipitant. Even with this small sample size, this is unlikely to explain the high rate of T-BPE occurring during bowel routines, particularly as five of the seven participants experiencing bowel-related T-BPE reported eight or fewer overall T-BPE in 48 hours. Bladder routines were often coded as occurring over a few or several minutes, as were other activities such as transfers. It was noted that many participants reported completing diaries after performing their bladder routines, potentially introducing a margin of error. It was suspected that some participants likely forgot to enter some routines based on long periods without entries and the typical intermittent catheterization schedule in this population. Further, 10 minute SBP measurement intervals when combined with diary entry errors may not capture or reflect actual SBP during bladder routines, particularly if dysreflexia arises during bladder filling, catheter insertion, or bladder evacuation.

Limitations

The frequency and severity of T-BPE appear to be clinically relevant in this study population. The individual application of these T-BPE results is dependent upon selection of baseline SBP thresholds. An artificially low or high baseline measurement would impact both the number and severity of T-BPE recorded. This appeared to be a factor in our study population, where one participant with a baseline SBP >30 mmHg below their 48-hour average and was excluded as an outlier. In particular, dehydration or other confounding events such as subclinical infection could easily have contributed to a false low value. The potential for participants with randomly elevated baseline pressures

Table 3 Proposed new terminology for classification of the severity of autonomic dysfunction, an extension of current hypertension terminology

Autonomic Dysreflexia/ Hypertension	Severity	Blood Pressure Threshold	Signs and Symptoms*
Autonomic Dysregulation	Autonomic Dysfunction	Transient 30–40 mmHg rise in SBP	No
	Autonomic Urgency/ *former Autonomic Dysreflexia*	Persistent 41–59 mmHg rise in SBP, ± a 10 bpm decline in HR	No/Yes
	Autonomic Emergency	Persistent increase in SBP of ≥ 60 mmHg ± a 10 bpm decline in HR	No/Yes (risk of end organ damage, including headache and/or chest pain)
Hypertension[19]	Hypertension	SBP > 140 mmHg or DBP > 90 mmHg	No
	Hypertension Urgency	SBP > 180 mmHg or DBP > 120 mmHg	No/Yes + end-organ damage
	Hypertension Emergency	SBP > 180 mmHg or DBP > 120 mmHg	Yes + end-organ damage

*Sign and Symptoms of Autonomic Dysreflexia[12] include;
- Pounding headache.
- Bradycardia (may be a relative slowing so that the heart rate is still within the normal range).
- Profuse sweating above the level of the lesion, especially in the face, neck, and shoulders, or possibly below the level of the lesion.
- Piloerection or goose bumps above or possibly below the level of the lesion.
- Cardiac arrhythmias, atrial fibrillation, premature ventricular contractions, and atrioventricular conduction abnormalities.
- Flushing of the skin above the level of the lesion, especially in the face, neck, and shoulders, or possibly below the level of lesion.
- Blurred vision.
- Appearance of spots in the visual fields.
- Nasal congestion.
- Feelings of apprehension or anxiety over an impending physical problem.

and omitted T-BPE must also be considered. Alternatives that may facilitate the study of T-BPE, should include multiple averaged SBP readings, or continuous blood pressure or heart rate monitoring over 24 hours, which are less sensitive to brief variations in SBP.

Each measurement consistent with a T-BPE was treated as a separate event, as it was not possible to determine whether consecutive T-BPE measurements reflected single or multiple episodes or single or multiple noxious or non-noxious stimuli. This was determined after graphing 48-hour blood pressure data highlighting that seemingly sequential events had interposed elevations below the T-BPE threshold, such as might be expected with a bowel program spanning several measurement intervals (30–60 minutes).

Potential correlates of T-BPE were assessed. Bowel routine data revealed a significant correlation between having a T-BPE during bowel care and the number of T-BPE with concurrent bradycardia. There is a clear need to develop a self-report electronic or voice activated tool for concurrent diarizing of clinical events which consistently and precisely identifies potential triggers of T-BPE. Incomplete diary entries and potential errors in the diary timelines may have skewed these results, despite coordinating the participants watch/ clock with the ambulatory monitor. With an expanded study, along with improved capture of bladder data, predictive modeling would likely allow for sufficient controlling of confounders to permit a more clinically applicable assessment of these relationships.

Clinical implications

The presence of T-BPE and the frequency and severity reported here suggest this as a prime target for further research to better understand their association with CVD risk and serve as a a potential intervention target for reducing CVD in individuals motor-complete tetraplegia or high-paraplegia living with chronic SCI. Refining the measures used, particularly the baseline SBP methodology, to define T-BPE frequency and duration, as well as exploring T-BPE predictors will constitute crucial next steps.

The data from this study although obtained from a small sample, offer the SCI community the opportunity to adopt new terminology for describing AD severity similar in nomenclature to that used in the hypertension community[19] with introduction of three terms: 1) *autonomic dysfunction* (transient 30–40 mmHg rise in SBP in the absence of symptoms); *autonomic urgency* formerly described as autonomic dysreflexia (persisitent 41–59 mmHg rise in SBP, and a ±10 bpm decline in HR with or without associated signs and symptoms);

and, *autonomic emergency* (persistent increase in SBP of ≥60mmHg and ± a 10 bpm decline in HR with or without associated signs and symptoms including headache and/or chest pain with a risk of end organ damage) (Table 3). Identifying the presence of these three distinct conditions, and the associated urgency or timelines for intervention, will assist in provision of clinical care, enable exploration of the associations between these distinct clinical entities, and CVD risk, thereby helping to facilitate clinical uptake of preventative measures once established.

Conclusion

This study has demonstrated that daily autonomic dysfunction, or transient blood pressure episodes (T-BPE), were common in this study population, with a majority of participants (13/19) experiencing T-BPE at a SBP elevation threshold of 40 mmHg. Many T-BPE were sufficiently severe to warrant therapeutic intervention. Several participants experienced "severe" (7/19) and even "extreme" (3/19) events, defined as elevations of ≥60 mmHg and ≥80 mmHg respectively. These events were corroborated through a secondary analysis, with a conservative T-BPE baseline (48-hour average SBP) and concomitant decrease of ≥10 bpm in heart rate. Twelve of 19 participants experienced T-BPE under this definition (at the 30 mmHg threshold), while 9/19 did so at the 40-mmHg threshold. The observed phenomenon appears to be of autonomic origin, and the frequency and severity of these events are likely of clinical significance. Given the conservative nature of the methods used, the significance of these T-BPE may be underestimated. The average 48-hour SBP (108 ± 10 mmHg) is in keeping with other studies in the SCI population.

Before applying these findings to individuals with SCI, the potential for varied numbers of T-BPE due to variability in baseline BP warrants attention. Observation from this study of supine averaged SBP (over 3 measures) suggests this to be subject to substantial short-term fluctuations. However, this was controlled in the secondary analysis through adoption of a 48-hour average SBP baseline, confirming the observed phenomenon regardless of baseline SBP. It may be possible to explore alternates such as composite average baseline SBPs. Surrogate markers of T-BPE, such as SBP variance, which are not sensitive to these baseline fluctuations may be a good alternative.

Importantly, it is unclear whether the severity of SBP elevation are best accounted for by the magnitude or duration of the SBP elevation. Further prospective longitudinal studies are required to determine the clinical associations with cardiovascular- morbidity and mortality based on the observed magnitude and duration of SBP elevations.

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Declarations

The authors have no conflict of interest. All authors were fully involved in the study design, data collection, analysis and preparation of the manuscript, and have provided their approval of the version to be submitted.

Disclaimer statements

Contributors None.

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Conflict of interest None.

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Disclosures None.

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